

CO-OCCURRENCE OF AGENESIS OF THE MAXILLARY LATERAL INCISORS WITH OTHER DENTAL ANOMALIES – A SYSTEMATIC REVIEW OF THE LITERATURE

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ABSTRACT

INTRODUCTION: Hypodontia of the maxillary lateral incisors is a developmental disorder whose genetic basis has been documented scientifically. Coexistence of hypodontia and other dental anomalies may indicate the occurrence of mutations within a given gene, the expression of which may be manifested in various phenotypic combinations.

OBJECTIVES: The aim of the study was to determine the frequency of co-occurrence of agenesis of the maxillary lateral incisors with other dental anomalies and skeletal disorders, based on a systematic review of the literature.

MATERIAL AND METHODS: An online database was searched using PubMed and Science Direct by entering the following keywords: maxillary lateral incisor agenesis and dental anomalies.

RESULTS: A total of 1168 results were obtained. Eighteen articles from 1971-2016 that met the inclusion criteria were qualified for the analysis. Hypodontia of the maxillary lateral incisors is very often accompanied by other dental or skeletal disorders. These are most often: agenesis of another permanent tooth, ectopic maxillary canine eruption, distoangulation of mandibular second premolars, reduction of the overall size of the teeth, the occurrence of a peg-shaped or microdontic maxillary lateral incisor, the rectangular shape of crowns of the maxillary central incisors, taurodontism. Skeletal class III is much more common than in the general population and the vertical relationship is also reduced. The most frequent was distal relation on the molars and canines.

CONCLUSIONS: Based on information obtained from medical databases and library resources, it can be concluded that hypodontia of the maxillary lateral incisors is a condition predisposing to the co-occurrence of other disorders: size, structure, position and quantity of remaining permanent teeth. When planning orthodontic treatment, attention should also be paid to the frequent prevalence of skeletal III in these patients and to the reduced vertical relationship.

KEY WORDS: maxillary lateral incisor agenesis, dental anomalies, systematic literature review.

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INTRODUCTION

Hypodontia is a disorder consisting in congenital absence of at least one deciduous or permanent tooth bud, while oligodontia is the absence of at least six tooth

buds excluding third molars [1]. The conducted studies have shown that the most frequently missing tooth is the mandibular second premolar (41%), then the lateral incisor in the maxilla (22.9%), in third place is the maxillary second premolar (21.2%) and fourth

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is the mandibular central incisor (3.5%) [2]. Hypodontia is one of the most common developmental disorders whose genetic background has been scientifically confirmed [3]. The results of a genetic study by Woolf [4] confirm his hypothesis that part of the genetic code in patients with agenesis of the maxillary lateral incisors consists of a dominant autosomal gene (or genes) that exhibits reduced penetration and variable expression. It is also likely that this feature may in some cases be recessive or have polygenic inheritance. Recent studies have found mutations in the genes *AXIN2*, *PAX9* and *MSX1* in families with hypodontia of permanent teeth [5, 6]. Other etiological factors of hypodontia and oligodontia include dental alveolar injuries, environmental factors such as rubella virus infection, action of chemical agents, medicines (e.g. thalidomide, chemotherapy) and radiotherapy [6]. The research carried out by Kjær [7, 8] confirms the hypothesis that disturbances in the tissues during the development process within the so-called fields of innervation may lead to agenesis of permanent teeth and most often the last teeth in the group are affected. The occurrence of hypodontia in deciduous teeth very often, but not always, correlates with the agenesis of their permanent successors [9]. Hypodontia and oligodontia are malformations that may be associated with other systemic or dental disorders [10-14]. Coexistence of hypodontia and other dental disorders such as ectopic canine eruption, microdontia, taurodontism and others confirms the genetic basis of the disorder and may indicate the occurrence of mutations within a given gene, whose expression may be manifested in various phenotypic combinations [13, 15, 16]. The incidence of maxillary lateral incisor agenesis (MLIA) is variable, depending on the studied population, and ranges from 2 to 5% [2, 16-18]. The incidence of MLIA is not sex dependent, and bilateral (68.9%) is more common than unilateral (31.1%) [16].

OBJECTIVES

The aim of the study was to determine the frequency of coexistence of agenesis of the maxillary lateral incisors with other dental anomalies and skeletal disorders, based on a systematic review of the literature.

MATERIAL AND METHODS

In order to determine the frequency of coexistence of agenesis of the maxillary lateral incisors with other dental anomalies and skeletal disorders, a systematic review of the literature was performed. An online database was searched using PubMed and Science Direct, using the following keywords: maxillary lateral incisor agenesis and dental anomalies. The analysis included randomized clinical trials, cohort studies and case-control studies, published until 2018. Case reports, literature

reviews, letters to the editor, articles in a language other than English and Polish and articles not directly related to the subject of the research were excluded.

RESULTS

A total of 1168 results were obtained, mainly in English. Literature taken from found articles was used to obtain additional research. Eighteen articles from 1971-2016, which met the inclusion criteria, were qualified for the further analysis, all in English. The analysis of results from separate studies is presented in Table 1.

ANALYSIS OF THE OBTAINED RESULTS

Citak *et al.* [16] found that hypodontia of the maxillary lateral incisors in 23.3% of cases was accompanied by agenesis of permanent teeth other than third molars. The study group consisted of 90 patients with confirmed hypodontia of the maxillary lateral incisors. In the Garib *et al.* [19] trial, among the 126 patients with hypodontia of the lateral incisors in the maxilla, 18.2% of the patients were diagnosed with hypodontia of other permanent teeth with the exclusion of third molars. This result was over three times higher than in the general population (results were compared by researchers with reference data obtained from other studies). The frequency of agenesis of other permanent teeth in patients with MLIA was: second maxillary premolars: 10.3% (general population: 1.5%), mandibular second premolars: 7.9% (general population: 3%), third molars: 35.5% (general population: 20.7%). There was no increased frequency in the occurrence of supernumerary teeth; it was 0.8%, a result lower than in the general population (1.5%), but it was not statistically significant. Celikoglu *et al.* [20] observed higher frequency of coexistence of agenesis of other permanent teeth (9.6%) in patients with MLIA in the Turkish population, where the co-occurrence of supernumerary teeth was only 1.1%, and this was not statistically significant. In the studies of Pinho *et al.* [21] hypodontia of other permanent teeth occurred in 12.8% of patients, with the most frequent being lack of second premolars both in the maxilla and the mandible (8.5%).

Citak *et al.* [16] noted a statistically significant increase in the incidence of a peg-shaped microdontic lateral incisor in patients with unilateral maxillary lateral incisor agenesis (15.6%) compared with the reference study. Celikoglu *et al.* [20] also observed that the unilateral agenesis of the lateral incisor is accompanied by a reduction in size or the presence of a conical contralateral incisor in 20.2% of cases. Another study conducted on a Jordanian patient population showed that as many as 50% of patients with unilateral MLIA have a reduced-width or conical opposite lateral incisor [22]. Results obtained by Stamatou and Symons [23] showed that the reduction or conical shape of the contralateral

TABLE 1. Coexistence of agenesis of the maxillary lateral incisors with other dental anomalies based on a systematic review of the literature

Position	First author, year	Country	MLIA group size	Associated anomalies
4	Woolf, 1971	USA	103	Peg-shaped maxillary lateral incisor – 23.3%
16	Citak, 2016	Turkey	90	Agenesis of other teeth – 23.3% Dens invaginatus – 1.1% Dens evaginatus – 2.2% Peg-shaped maxillary lateral incisor – 15.6% Taurodontism – 42.2% Pulp stone – 10.0% Dilaceration – 18.9% Impaction of maxillary canine – 5.6%
18	Baidas, 2005	Saudi Arabia	30	Small lateral incisor Small central incisors Bolton index – maxillary insufficiency
19	Garib, 2010	Brazil	126	Tooth agenesis – 18.2% Maxillary second premolar agenesis – 10.3% Mandibular second premolar agenesis – 7.9% Third molar agenesis – 35.5% Supernumerary teeth – 0.8% Small maxillary lateral incisor – 38.8% Palatally displaced canine – 5.2% Mandibular second premolar distoangulation – 3.9% Mandibular second molar mesioangulation – 0.0%
20	Celikoglu, 2012	Turkey	94	Ectopic eruption of maxillary canine – 21.3% Reduced or peg-shaped maxillary lateral incisor – 20.2% Hypodontia of other teeth – 9.6% Dilaceration – 6.3% Impaction of maxillary canine – 5.3% Maxillary lateral incisor – canine transposition – 1.1% Transmigration of maxillary canine – 1.1% Supernumerary tooth – 1.1% Skeletal class I – 55.3% Skeletal class II – 16.0% Skeletal class III – 28.7%
21	Pinho, 2005	Portugal	219	Hypodontia of other teeth – 12.8% Hypodontia of second premolar – 8.5% Reduced or peg-shaped maxillary lateral incisor – 59.5%
22	Albashaireh, 2006	Jordan	20	Reduced or peg-shaped maxillary lateral incisor – 50.0%
23	Stamatiou, 1991	Australia	91	Reduced or peg-shaped maxillary lateral incisor – 33.0%
25	Yaqoob, 2011	United Kingdom	52	Small anterior teeth width – mean discrepancy 0.42 mm per tooth in upper and 0.33 mm per tooth in lower anterior segments
26	Mirabella, 2012	Italy	81	Smaller teeth width (from 0.11 to 0.49 mm) Microdontic contralateral maxillary lateral incisor – 44.9%
27	Olivadoti, 2009	Italy	31	Maxillary central incisors smaller by about 0.38 mm at contact points, change of shape of central incisors – more rectangular
28	Wright, 2016	USA	40	Small overall teeth width, in males posterior teeth in females anterior teeth more often Microdontic contralateral maxillary lateral incisor about 1.27 mm smaller than in control group
29	Al-Nimri, 2011	Jordan	246	Palatally displaced canine – 12.6% Class I malocclusion – 42.3% Class III malocclusion – 25.2% Class II Div 2 malocclusion – 20.3% Class II Div 1 malocclusion – 12.2%
30	Becker, 1981	Israel	88	Palatally displaced canine – 5.5%

TABLE 1. (Continued)

Position	First author, year	Country	MLIA group size	Associated anomalies
31	Pinho, 2011	Portugal	147	Deviation of the maxillary dental midline Molar and canine class II relationship
33	Woodworth, 1985	USA	43	Craniofacial deviations from normal: smaller maxillary length, smaller mandibular length, smaller anterior cranial base, nasal bone, smaller vertical dimensions (anterior and posterior), smaller mandibular plane angle, 10° greater nasolabial angle
34	Pinho, 2011	Portugal	147	Shortening of the maxilla Reduced anterior facial height
35	Bassiouny, 2016	Saudi Arabia	52	Significant tendency for skeletal class III Maxillary hypoplasia/retrognathia

incisor occurs in 33% of patients with unilateral form of MLIA. Researchers highlight the genetic basis of this condition. Also, Pinho *et al.* [21] demonstrated a reduction in the dimensions of the lateral incisor of the opposite side in 59.5% of patients. The Woolf [4] study showed that in 23.3% of patients with unilateral MLIA there is a conical shaped contralateral lateral incisor. In the study of Garib *et al.* [19] with unilateral agenesis of the maxillary lateral incisor, the size of the crown of the incisor of the opposite side is decreased (38.8%). This result was very high compared to the reference studies carried out in 1998 by Bacetti [24], which estimated the incidence of this defect in the general population at 4.7%. Baidas and Hasim [18], when measuring the width of individual teeth and analysis of the Bolton anterior index, found that in patients with unilateral MLIA, the width of the lateral incisor of the opposite side is 1 mm lower than the standard (5.5 mm, with the standard of 6.5 mm accepted by researchers). Maxillary central incisors showed a reduction in width. Analysis of the Bolton anterior index showed the reduction of dental material, both in the case of bilateral and unilateral form of MLIA. Also, a study conducted by Yaqoob *et al.* [25] confirmed the reduction in the overall tooth size in patients with bilateral agenesis of the maxillary lateral incisors compared to the control group, which comprised fully dentate patients. The difference was noticeable in both the upper and lower dental arch. Researchers compared the width of six front teeth. The mean values resulting from the measurements of the maxillary teeth width in MLIA patients revealed a reduction in the dimensions of each tooth by an average of 0.42 mm, and in the case of mandibular teeth they were smaller by an average of 0.33 mm. Similar results, however, considering the width of 12 teeth in both the maxilla and the mandible, were obtained by Mirabella *et al.* [26]. Their study showed that the width of permanent teeth in patients with both unilateral and bilateral hypodontia of the maxillary lateral incisors is on average 0.11 to 0.49 mm per tooth lower than in the control group with full permanent dentition. Only the maxillary first molars

did not show a reduced size. There was no difference in crown width compared to the control group in patients with bilateral and unilateral hypodontia of the maxillary lateral incisors. Researchers also evaluated the prevalence of the microdontic opposite side lateral incisor in patients with unilateral MLIA. The frequency of the abovementioned anomaly was 44.8%. Mirabella *et al.* [26] also underlined the fact of the MLIA genetic background. According to the researchers, the gene, causing hypodontia of the maxillary lateral incisors, reduces the total dimensions of the teeth. The authors emphasized how important from a clinical point of view the research they conducted is. The front teeth, due to the reduced size, will often require aesthetic restoration to ensure efficient occlusion and good aesthetics, both in the opening of space for the future prosthetic or implant prosthetic restoration as well as in the orthodontic closure of the spaces. Another important clinical study is the work of Olivadoti *et al.* [27]. They assessed the shape and width of maxillary central incisors at the contact points and in the 1/3 gingival. The obtained results indicated a reduction in the dimensions of these teeth in patients with MLIA at the level of contact points by an average of 0.38 mm, in the absence of a significant reduction in the width in 1/3 gingival. This indicated a change in the shape of the central incisors to more rectangular ones. Researchers emphasize the need for aesthetic correction of the shape of these teeth in patients with MLIA. Wright *et al.* [28] measured the width of the teeth in 40 patients with unilateral and bilateral hypodontia of the lateral incisors. The results indicated a reduction in the dimensions of the teeth. In men with MLIA, the lateral teeth were 0.28 mm to 0.78 mm smaller than the control group, and women showed a reduction in the dimensions of the anterior teeth by 0.22 mm to 0.42 mm. In cases of unilateral MLIA, the contralateral incisor showed an average width of 5.39 mm, compared with the average width of the maxillary lateral incisors in the control group of 6.66 mm, which gave a difference of 1.27 mm. Co-occurrence of the conical tooth was also more frequently observed.

Garib *et al.* [19] found an increased frequency of palatally displaced canines (PDC) in patients with hypodontia of the lateral incisors in maxilla at 5.2%, which was statistically significant. Citak *et al.* [16] did not report a higher incidence of impacted canines in patients with MLIA (5.6%). The results obtained in both studies are similar to each other, and the difference in their interpretation may be caused by differences in the values in the reference data and the size of the studied groups. In the Garib *et al.* [19] trial, the incorrect positioning of other permanent teeth was also assessed: distoangulation of second premolars in the mandible (3.9% in patients with MLIA, and only 0.2% in the reference study of the general population) and mesial inclination of the second molar in the mandible (no statistically significant differences). Al-Nimri and Bsoul [29] found a positive correlation between the occurrence of palatally impacted canines and the agenesis of the lateral incisors in the maxilla. The study group consisted of 246 patients with single or bilateral maxillary lateral incisor agenesis. In 12.6% of patients PDC coexisted with maxillary lateral incisor agenesis. However, there was no greater risk of occurrence of palatally impacted canines in patients with bilateral hypodontia of the lateral incisors compared to the unilateral form. According to the researchers, the high percentage of coexistence of both disorders may confirm the guidance theory, according to which the distal part of the root of the maxillary lateral incisor leads the canine bud in the right direction during its long eruption path. The study is in line with the results obtained by Becker *et al.* [30], who also found a positive correlation between PDC and MLIA (5.5% of 88 patients with PDC showed agenesis of the maxillary lateral incisors). Celikoglu *et al.* [20], investigating the co-occurrence of dental anomalies with hypodontia of the maxillary lateral incisors, observed that in a group of 94 patients with MLIA, 66% of patients suffer from structural defects, size, number or tooth position disorders. Ectopic canine eruption occurred in 21.3% of patients with MLIA. There were 5.3% of patients with canine impaction, but the result was not statistically significant. Transmigration of the maxillary canines occurred only in 1.1% of patients.

Citak *et al.* [16] stated that the frequency of MLIA coexistence with the presence of dens invaginatus and evaginatus is respectively 1.1 and 2.2%. This result was not statistically significant and did not differ from the general population. Also, the incidence of pulp stones was not greater in patients with maxillary lateral incisor agenesis. However, there was a statistically significant increased frequency of taurodontic teeth in patients with MLIA and it was 42.2%. Dilaceration of the root was also more common (18.9%) than in the general population (9.5%). Celikoglu *et al.* [20] studies have shown that in patients with MLIA, the coexistence of root dilaceration occurs at the level of 6.3%, but this result was not statistically significant for the population of patients

with full dentition. The abovementioned coincidence of the shape disorder of the lateral incisor of the opposite side in patients with unilateral form of MLIA, often being at the same time a form of the abnormal shape of this tooth (conical tooth), has been underlined by researchers in several works [4, 16, 22, 23]. This anomaly occurred in 15.6% up to 23.3% of patients with unilateral agenesis of the maxillary lateral incisor.

Al-Nimri and Bsoul [29] stated that among patients with hypodontia of maxillary lateral incisors, the most common was class I malocclusion (42.3%), the second was class III malocclusion (25.2%), then class II subgroup 2 malocclusion (20.3%). The most rarely observed was class II subgroup 1 malocclusion (12.2%). Pinho and Lemons [31] observed that in patients with unilateral and bilateral agenesis of maxillary lateral incisors, the deviation of the upper dental midline is common (in cases of unilateral agenesis, to the affected side) and the distal relationship is most often found on the molars and canines. A study by Celikoglu *et al.* [20] in which skeletal class was assessed in patients with aplasia of the maxillary lateral incisors showed that in MLIA patients skeletal class I was most common (55.3%), followed by skeletal class III (28.7%), and the least frequent skeletal class II (16%). There was also an increased incidence of skeletal class III in patients with MLIA with reference to the general population. In patients with agenesis, skeletal class III occurred in as many as 28.7%, and in the general population in 11.5% [20, 32]. Woodworth *et al.* [33], comparing cephalograms of patients with hypodontia of the maxillary lateral incisor with the norm, found that in patients with MLIA there occurs reduced length of the maxilla and mandible, reduced anterior cranial base, and shortened nasal bone. There was also a decrease in the vertical relationship, both anterior and posterior face height, and reduction in the mandibular plane angle. Analysis of soft tissues showed that in patients with MLIA the value of the nasolabial angle was on average 10° lower than the recognized norm. Researchers found that the results obtained gave a general picture very similar to those of cleft patients and this may indicate a weaker development of the craniofacial structures in these patients. Pinho *et al.* [34] also evaluated the effects of maxillary lateral incisor agenesis on skull structures in their studies. Their results confirmed the results obtained by Woodworth *et al.* [33]. The length of the maxilla was observed to be reduced (the measurement was made between the ANS-PNS points) and the facial height also was reduced. However, MLIA did not correlate with the change in the inclination of the palatal plane relative to the Frankfurt plane. A study by Basiouny *et al.* [35] showed that patients with congenital lack of maxillary lateral incisors have a significant tendency to skeletal class III. The researchers attribute these results to the occurrence of maxillary hypoplasia (retrognathia) in these patients.

CONCLUSIONS

Based on information obtained from medical databases and library resources, it can be concluded that hypodontia of the maxillary lateral incisors is a condition predisposing to the co-occurrence of other disorders: size, structure, position and quantity of other permanent teeth. The distal molar and canine relationship was the most common. Studies carried out so far in Europe and worldwide indicate the genetic basis of the problem. Coexistence of the agenesis of permanent teeth, especially the maxillary lateral incisors, was observed in patients with ectopic canine eruption [29, 36]. The frequent lack of maxillary lateral incisors in patients with ectopic eruption, palatally displaced or impacted canines, confirms both guidance and genetic theories, which are cited as potential explanations of this condition [30, 37]. From a clinical point of view, it is extremely important that patients with early-detected maxillary lateral incisor agenesis should be able to check both the radiological and clinical process of maxillary canines' eruption, as it can be stated on the basis of the analysis of the referenced data that they are patients at risk of palatal retention of these teeth. In such cases, it may be necessary to conduct interceptive treatment involving the extraction of the deciduous maxillary canines at the appropriate stage of development [38-40]. Based on the systematic review of the literature it can be concluded that patients with maxillary lateral incisor agenesis also have a decrease in mesio-distal crown dimensions of permanent teeth, especially the anterior teeth, and the crowns of the maxillary central incisors most often have a rectangular shape. For this reason, very often the anterior teeth of patients with MLIA will require an aesthetic shape correction and increase in width. The analysis of the conducted studies also showed that in patients with MLIA, skeletal class III was more frequent than in the general population, shortening the length of the maxilla, and a decrease in the vertical relationship was also noted. Our own study [41] confirmed that the congenital lack of maxillary lateral incisors is one of the symptoms indicating a maxillary deficiency syndrome. So far, no studies showing the frequency of coexistence of the disorders discussed above have been carried out in patients with MLIA in the Polish population.

CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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